REMARKS

Attached hereto is a marked up version of the changes made to the claims by this amendment. The attachment is captioned "**Version With Markings to Show Changes Made.**"

In response to the rejections raised by the Examiner in the January 14, 2002 Office Action, our comments follow. Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the amendments and remarks herewith, which place the application into condition for allowance or into better condition for appeal.

The Examiner, Primary Examiner Navarro and SPE Smith are thanked for courtesies extended during the telephonic interview on February 7, 2002.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1 and 13 have been amended. Support for the amended claims can be found throughout the specification and particularly on page 7, lines 28-29 and on page 8, lines 23-28. Claims 55-56 have been added; claims 51-54 have been cancelled. Claims 1-21, 29-31 and 55-56 are now pending. No new matter is added by these amendments.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. §112. The amendments of and additions to the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Support is found throughout the specification and from the pending claims.

II. THE REJECTION UNDER §103 IS OVERCOME

Claims 1-21 and 29-31 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Braig *et al.*, in view of Holland *et al.* As was discussed by the undersigned and the Examiners in the February 7, 2002 interview, the instant invention is distinguishable over the cited references because neither reference provides any incentive or suggestion to a person skilled in the art to utilize the fragments of GroEL as taught in the present application. Braig *et al.* do not teach or suggest that fragments of the GroEL sequence disclosed therein may be made, or that such fragments would have chaperone activity. Further, Braig *et al.* do not teach or suggest fusion polypeptides. Although Holland *et al.* teach a process of making recombinant

fusion polypeptides, they do not teach or suggest the use of GroEL polypeptides or fragments thereof.

Moreover, the present invention is not obvious to one of skill in the art since neither Braig *et al.* nor Holland *et al.* teach chaperone polypeptides in which positions 262 and 267 are not occupied by alanine and isoleucine, respectively, as is now recited in amended claims 1 and 13. As described in the paragraph bridging pages 7 and 8 of the application, fragments of the GroEL sequence in which positions 262 and 267 are occupied by alanine and isoleucine, respectively, are inoperative and unable to promote folding of polypeptides. Thus, a fragment of the polypeptide disclosed by Braig *et al.* that included an alanine and isoleucine residue at positions 262 and 267, respectively, would not demonstrate "chaperone activity", as defined on page 8, lines 23-28, and could not be defined as a "chaperone polypeptide", as required by the claims. Therefore, even if the skilled artisan were motivated by Braig *et al.* in view of Holland *et al.* to make a GroEL fusion polypeptide using fragments based on the sequence disclosed by Braig *et al.*, which is not admitted, the fragment/fusion polypeptide would not have chaperone activity and thus the skilled artisan would not arrive at the presently claimed invention.

It should be noted that claim 1 has been amended to recite the refolding activity of the chaperone polypeptide. Functional activity in claim 1 has not been limited to a refolding activity of greater than 50%, as in claim 13, to avoid unnecessarily and unfairly limiting the scope of protection to which the Applicants are entitled. For example, page 45, lines 9-11 of the specification teach that GroEL fragment 191-345 has a rhodanese refolding activity of 42.5%, which represents an 8.5-fold increase in refolding activity over background refolding.

The preceding arguments demonstrate that claims 1-21 and 29-31 are not obvious. Reconsideration and withdrawal of the Section 103 rejection is believed to be in order and such action is respectfully requested.

CONCLUSION

In view of the remarks and amendments herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,

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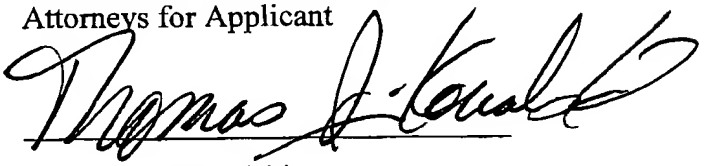

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Version with Markings to Show Changes Made

IN THE CLAIMS

1. (Thrice Amended) A chaperone polypeptide having refolding activity and having an amino acid sequence selected from at least amino acid residues 230-271 but no more than residues 150-455 or 151-456 of a GroEL sequence as shown in Figure 7, wherein positions 262 and 267 are occupied by amino acid residues other than alanine and isoleucine, respectively, or a corresponding sequence of a chaperone polypeptide, said corresponding sequence sharing at least 50% homology with said amino acid sequence.

13. (Twice amended) A monomeric polypeptide, having chaperone activity and incapable of multimerisation, characterised in that, in the absence of ATP, the polypeptide has a protein refolding activity of more than 50%, said refolding activity being determined by contacting the polypeptide with an inactivated protein of known specific activity prior to inactivation, and then determining the specific activity of the said protein after contact with the polypeptide, the % refolding activity being:

$$\frac{\text{specific activity of protein after contact with polypeptide x 100}}{\text{specific activity of protein prior to inactivation}} \quad 1$$

wherein the selected amino acid sequence is selected from the group consisting of 230-271, 191-345, 191-376, 193-335 and 193-337 of GroEL, wherein positions 262 and 267 are occupied by amino acid residues other than alanine and isoleucine, respectively, or a corresponding sequence of a chaperone polypeptide, said corresponding sequence sharing at least 50% homology with said amino acid sequence.